

# Genes-4U

## Platelet Glycoprotein IIIA T393C (HPA-1 a/b = PI<sup>A1</sup>/PI<sup>A2</sup>)

The **HPA-1 epitope** is found on glycoprotein IIIa (GPIIIa). The single nucleotide transition from **T to C at nucleotide 393 of the GPIIIa gene** causes a substitution of leucine to proline at amino acid residue 33 of GPIIIa, converting **HPA-1a (PI<sup>A1</sup>) to HPA-1b (PI<sup>A2</sup>)** (1). Although the function of GPIIIa is not profoundly affected, this change alters the antigenic properties of the molecule.

Platelet membrane glycoproteins can be targets for alloimmune antibody responses that cause bleeding disorders. In post-transfusion purpura (PTP), a transfused patient forms alloantigen-specific antibodies, that, for still unknown reasons, may cause destruction of autologous platelets often resulting in life-threatening thrombocytopenia. In fetomaternal alloimmune thrombocytopenia, designated as neonatal alloimmune thrombocytopenic purpura (NATP), fetal thrombocytopenia is caused by maternal alloimmunization against one or more paternal platelet alloantigens and is a significant cause of morbidity.

**The determinant implicated in the pathogenesis of most reported cases of PTP and NATP is human platelet antigen -1a (HPA-1a, PI<sup>A1</sup>)** (2).

Severe NATP may lead to either prenatal or neonatal intracranial haemorrhage that may cause fetal death or psychomotor impairment. NATP occurs in one out of 1200 births of which > 40% are firstborns. 87% of subsequent pregnancies in those families are also affected. Typing of human platelet alloantigens is also necessary for the investigation of platelet refractoriness due to platelet-specific antibodies and in the provision of the appropriate antigen-negative platelets for alloimmunized patients.

It is also of interest that HPA-1a has recently been proposed as an inherited risk factor for coronary thrombosis, premature myocardial infarction and coronary stent thrombosis (3).

Immunophenotyping of the HPA-1 system has several drawbacks, including the need for sufficiently high platelet counts, shortages of typing antisera, and a time-consuming procedure. **Therefore genotyping of platelet antigens has become a preferred procedure.**

## References

(1) Newman, P.J., Derbes, R.S. & Aster, R.H. (1989) The human platelet alloantigens, PIA1 and PIA2, are associated with a leucine33/proline33 amino acid polymorphism in membrane glycoprotein IIIa, and are distinguishable by DNA typing. *Journal of Clinical Investigation*, **83**, 1778–1781

(2) Williamson, L.M., Hackett, G., Rennie, J., Palmer, C.R., Maciver, C., Hadfield, R., Hughes, D., Jobson, S. & Ouwehand, W.H. (1998) The natural history of fetomaternal alloimmunization to the platelet-specific antigen HPA-1a (PIA1, Zwa) as determined by antenatal screening. *Blood*, **92**, 2280–2287.

(3) Zotz, R.B., Winkelmann, B.R., Nauck, M., Giers, G., Maruhn-Debowski, B., Marz, W. & Scharf, R.E. (1998) Polymorphism of platelet membrane glycoprotein IIIa: human platelet antigen 1b (HPA-1b/PIA2) is an inherited risk factor for premature myocardial infarction in coronary artery disease. *Thrombosis and Haemostasis*, **79**, 731–735.